UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/814,604	03/22/2001	Elliott S. Klein	P-AR 4528	4120

23601 7590 03/08/2004

CAMPBELL & FLORES LLP
4370 LA JOLLA VILLAGE DRIVE
7TH FLOOR
SAN DIEGO, CA 92122

EXAMINER	
MURPHY, JOSEPH F	
ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 03/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/814,604	KLEIN ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Claims 1-26 are pending and under consideration.

Specification

The abstract of the disclosure is objected to because it is entitled "Abstract of the Invention". Pursuant to 37 CFR 1.72 a brief abstract of the technical disclosure in the specification must commence on a separate sheet, preferably following the claims, under the heading "Abstract " or "Abstract of the Disclosure". Correction is required. See MPEP § 608.01(b).

Response to Amendment

The rejection of claims 1-26 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for being vague and indefinite in the recitation of the phrase "test complex".

The rejection of claims 1-26 under 35 U.S.C. 102(b) as being anticipated by DiRenzo et al. (1997) has been withdrawn.

The rejection of claims 1-26 under 35 U.S.C. 103(a) as being unpatentable over DiRenzo et al. (1997) has been withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2, 11 and 18 are vague and indefinite in the recitation of the term "activities". This term is not clearly defined in the claims. The specification also does not clearly define the term, but it seems to include, *inter alia*, an indirect signaling pathway activated by the nuclear hormone receptor, and on other nuclear hormone receptor mediated pathways (page 9, lines 5-20), and also a decrease in interaction with corepressors and an increase in interaction with coactivators (page 14, lines 10-20). Thus, since the term "activities" includes effects on indirect pathways not directly associated with nuclear hormone receptor function, the skilled artisan would not be apprised of the metes and bounds of the functional limitation with regard to the activities which are dissociated. Claims 3-10, 12-17, 19-26 are rejected insofar as they depend on the recitation of the term "activities" in claims 1, 2, 11, 18

Applicant argues that as set forth in the specification, nuclear receptor activities include the effects of hormone receptor mediated pathways indirectly activated by ligand as well as direct activation of transcription. The specification teaches, for example, that ligands that dissociate nuclear hormone receptor activities have selective indirect effects through nuclear hormone receptor-mediated pathways while failing to directly activate transcription through cognate response element (page 9, lines 2-13). The metes and bounds of this term

cannot be determined based upon the definition provided in the Specification because the activities ascribed to the nuclear hormone receptor are exemplary, and further there is no indication what the indirect effects would be.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 6-8, 11-13, 16, 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al. (1995).

The claims are drawn to methods of identifying agents which dissociate nuclear hormone "activities" the steps comprising addition of an agent to a test complex comprising a nuclear hormone receptor, a coactivator, a corepressor (claim 1), and/or the addition of a nuclear hormone response element (claim 2), and measuring the dissociation of an "activity" upon addition of the agent. The comparison to TTNPB is only necessary if the nuclear hormone is RAR. Chen et al. report the identification of a receptor-interacting factor, SMRT, as a silencing mediator (co-repressor) for retinoid and thyroid-hormone receptors. SMRT is a previously undiscovered protein whose association with receptors both in solution and bound to DNA-response elements is destabilized by ligand (Chen at 454, column 2, third paragraph). In the Chen reference, on page 456, Figure 3, a method is presented in which the interaction of SMRT with receptor-DNA complex in the presence of PAF, as coactivator (page 457, column 2 second paragraph). Claims 1-2, 16, 19 are anticipated because the method identifies an agent (ligand)

which dissociate nuclear hormone "activities" the steps comprising addition of an agent to a test complex comprising a nuclear hormone receptor (TR), a coactivator (PAF), a corepressor (SMRT), in the presence of a nuclear hormone response element (the oligo probe). Claims 3, 6-8 are anticipated because the reaction is carried out in vitro, in a reticulocyte lysate. Claims 11-13 are anticipated because the method is carried out with RXR-RAR or TR.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 6-8, 11-16, 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (1995) in view of Chen et al. (1996).

The claims are drawn to methods of identifying agents which dissociate nuclear hormone "activities" the steps comprising addition of an agent to a test complex comprising a nuclear hormone receptor, a coactivator, a corepressor (claim 1), and/or the addition of a nuclear

hormone response element (claim 2), and measuring the dissociation of an "activity" upon addition of the agent. The comparison to TTNPB is only necessary if the nuclear hormone is RAR. Chen et al. report the identification of a receptor-interacting factor, SMRT, as a silencing mediator (co-repressor) for retinoid and thyroid-hormone receptors. SMRT is a previously undiscovered protein whose association with receptors both in solution and bound to DNA-response elements is destabilized by ligand (Chen at 454, column 2, third paragraph). In the Chen reference, on page 456, Figure 3, a method is presented in which the interaction of SMRT with receptor-DNA complex in the presence of PAF, as coactivator (page 457, column 2 second paragraph). Chen et al. does not teach the coactivator as being SRC-1. The Chen (1996) reference teach that the effect of hormone in nuclear receptor signaling is to relive silencing by inducing a dissociation of corepressor and to activate transcription by recruiting transcriptional coactivator(s) such as Trip1, RIP140, RIP160, TIF1 and SRC-1 (page 7570, column 2, second paragraph). The motivation is provided in the Chen (1996) reference that teaches that transcriptional silencing has been shown to play an important role in development, cell differentiation and cellular transformation (page 7570, second column, second paragraph).

Conclusion

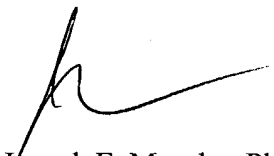
No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Murphy whose telephone number is (571) 272-0877. The examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571) 272-0871.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
February 26, 2004